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[REDACTED] EXAMINER

SLOBODYANSKY, ELIZABETH

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1652

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	DAVIS ET AL.
Examiner	Art Unit
Elizabeth Slobodyansky, PhD	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 20 February 2004.
2a) This action is FINAL. 2b) This action is non-final.
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 18-34, 36, 38-42, 44-68 and 70 is/are pending in the application.
4a) Of the above claim(s) 18-34, 46-68 and 70 is/are withdrawn from consideration.
5) Claim(s) _____ is/are allowed.
6) Claim(s) 36, 38-42, 44 and 45 is/are rejected.
7) Claim(s) _____ is/are objected to.
8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) Notice of Informal Patent Application (PTO-152)
6) Other: _____.

DETAILED ACTION

The amendment filed February 20, 2004 amending claims 36, 38, 39, 41 and 44 and canceling claims 37 and 43 has been entered.

Claims 18-34, 36, 38-42, 44-68 and 70 are pending. Claims 18-34, 46-68 and 70 are withdrawn.

Claims 36, 38-42, 44 and 45 are under consideration.

It is noted that claim 45 has been indicated in the amendment as "withdrawn" (page 3). This appears to be a typographical error. For the purpose of this examination, claim 45 (dependent from claim 36) was included in the scope of the examined claims.

Specification

The instant disclosure contains sequence disclosure that is encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, while the computer readable form (CRF) contains the correct information reading the application data, the paper copy is a copy from the parent case. Applicants are required to submit the paper copy of the Sequence Listing containing the updated application data together with a statement that it is identical to the CRF present in the file. **No CRF** is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36, 38-42, 44 and 45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Amended claim 36 is drawn to "a method for assaying a chemically modified mutant enzyme, said method comprising: a) providing a swatch of material comprising a piece of material and a protein stain; b) fixing the protein stain to the material with a crosslinking agent; c) applying a chemically modified mutant enzyme to the swatch; and d) incubating the swatch and the chemically modified mutant enzyme.

Therefore, claim 36 recites a genus of chemically modified mutant enzymes, a genus of materials, a genus of protein stains and a genus of crosslinking agents. Each of these genera encompasses unlimited number of compounds and materials. Enzymes are an enormous group of proteins both naturally-occurring and man made with totally different structures, effects and utilities. Enzymes comprise different sequence wherein each residue and/or all residues can be chemically modified. Materials are an enormous group of unrelated materials both naturally-occurring and man made such as different types of textile, ceramic, wood, etc. Crosslinking agents are a genus of chemically unrelated compounds having different structures, effects and utilities such as hydrogen peroxide, glutaraldehyde, glyoxal, succinaldehyde, etc. The specification does not describe any crosslinking agent used for fixing the protein stain to the material.

It is apparent that each given protein stained swatch requires a specific crosslinking agent and a specific chemically modified mutant enzyme to remove the

stain. The specification does not teach the correlation among genera of protein stains, materials, chemically modified enzymes and crosslinking agents and does not teach the correlation between the structure and function within each genus.

Claim 38 limits a chemically modified mutant enzyme to a protease, a cellulase, an amylase, a laccase and a lipase. Each of them encompasses a distinct genus of enzymes. Claim 39 recites a chemically modified mutant hydrolase wherein one or more amino acid residues in the hydrolase are replaced by cysteine residues, wherein the cysteine residues are modified by replacing the thiol hydrogen in said cysteine residues with a substituent group providing a thiol side chain comprising a multiply charged moiety. Hydrolases are a class of enzymes comprising several families of enzymes with different structures, catalytic action and effects. They include several families of enzymes such as proteases. Even a genus of proteases encompasses enzymes with different structures and functions. Claims 39 limits neither the starting unmodified enzyme nor mutations, chemical modifications and function.

The specification teaches a chemically modified mutant (CMM) of a protease, *Bacillus lenthus* subtilisin (SBL) obtained by replacement of an amino acid residue with various alkyl and mono-, di- and triammonium groups using methanethiosulfonate (MTS). The specification teaches that said variants can be used in washing blood/milk/ink swatches (pages 26-27).

The specification fails to describe any other representative species of chemically modified mutant proteases or other enzymes, protein stains and materials.

As mentioned above each residues in the amino acid sequence of an enzyme can be mutated and each residue can be chemically modified. The properties of the chemically modified mutant enzyme depend on the structure of the parent unmodified enzyme, the residue(s) that is (are) modified and the nature of chemical modification. The specification provides no teaching as to correlation between the structure of a chemically modified mutant enzyme and its function. Therefore, the genus of chemically modified mutant enzymes is an enormous highly variable genus.

When, like in the instant case, there is great variation within each genus, one must describe a sufficient variety of species to reflect the variation within the genus. Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed.

Thus, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims not specifically discussed above are rejected as dependent from the rejected base claim.

Claims 36, 38-42, 44 and 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of use of the specific

chemically modified mutant enzyme (CMM) of SBL with a protein stained swatch, does not reasonably provide enablement for a method of use of said CMM SBL or any CMM enzymes with other protein stains and materials and for a method of use of the specific CMM SBL of the invention or CMM enzyme with any protein stain crosslinked to a material. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir., 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 36, 40-42, 44 and 45 encompass any chemically modified mutant enzyme. Claim 38 limits chemically modified mutant enzymes to a protease, a cellulase, an amylase, a laccase and a lipase. Claim 39 encompasses any chemically modified mutant hydrolase. The specification does not teach the correlation among a protein stain, a material, a crosslinking agent and a chemically modified mutant enzyme. While the art enables the use of a protease to remove a protein stain from a textile swatch, a lipase to remove oil, an amylase to remove starch, for example, there is no teaching in the art or guidance in the specification as to how to remove a protein stain with a lipase,

for example, i.e. how to use an enzyme of any specificity with any stain and material. With regard to claims 41 and 42, there is no guidance as to what enzyme should be used with a given stain or which protease other than subtilisin should be used to remove blood/milk stain. There is no teaching as to what enzyme removes ink. Further, the claims encompass a step of fixing a protein stain with a cross-linking agent. The specification does not teach a cross-linking agent used for said purposes and does not provide guidance as to why a stain should be additionally crosslinked when the purpose of the procedure is its removal. It is clear that each combination of protein stain and material requires its own pool of enzymes from which the preferred enzyme, i.e. the enzyme having the high performance in removing the given stain from a specific material is chosen. The guidance provided by the specification is at most limited to the specific CMMs of SBL and blood/milk stain on a cotton swatch. Furthermore, the specification does not teach how to remove a protein stain that is crosslinked to a swatch by any crosslinking agent with any enzyme including CMM SBL specifically taught by the specification.

The art teaches that finding an enzyme useful for removal of a specific stain from a given material is a matter of trial and error.

Thus, searching for an enzyme useful in any application is well outside the realm of routine experimentation and predictability in the art of success is extremely low.

Therefore, one skilled in the art would require guidance beyond that provided in the specification as to how to make an enzyme useful for removal of any stain or crosslinked stain from any material and how to use a CMM of SBL for removal of stains

other than blood/milk on cotton swatches. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36, with dependent claims 38-42, 44-45, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36 is incomplete as omitting essential steps such as the step of washing after incubating, for example, and conditions under which washing is carried out before determining the degree of removal of the protein stains.

Response to Arguments

Applicant's arguments filed February 20, 2004 have been fully considered but they are not persuasive.

It is noted that original Claim 36 was drawn to "a method for assaying for a preferred enzyme" whereas claim 36 as amended February 20, 2004 is drawn to "a method for assaying a preferred ... enzyme". While such amendment can be made the changes to the claim should have been indicated.

With regard ton the 112, 1st and 2nd paragraphs rejections, Applicants state amended claim 36 satisfies the requirement of USC 35 112, 1st paragraph, without explaining the reasons for said conclusion.

With regard to 102 and 103 rejections they have been withdrawn in view of the amendment to claim 36 that now recites crosslinking of the protein stain to the material. However, as noted above, the specification does not teach any crosslinking agent used for fixing the protein stain to the material rendering the claimed methods neither described nor enabled.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

May 14, 2004